OPINION ARTICLE
ARTIGO DE OPINIÃO

Risk Sharing Agreement: a pilot project in the Brazilian Unified Health System

Acordo de Compartilhamento de Risco: projeto-piloto no Sistema Único de Saúde

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ABSTRACT

Risk Sharing Agreement is defined as an agreement in which the State agrees to offer temporary access to a new drug, while the pharmaceutical industry accepts to receive the product according to the performance of the drug in real conditions of use. Risk sharing necessarily depends on the collection of additional evidence that may refer to the therapeutic benefits or the volume of patients, according to the assessment of its use in practice. The authors described the experience of the pilot project of a Risk Sharing Agreement in the Unified Health System.

Palavras-chave:
contrato de risco, participação no risco financeiro, avaliação da tecnologia biomédica

RESUMO

O Acordo de Compartilhamento de Risco é definido como um acordo no qual o Estado concorda em oferecer acesso temporário a um novo medicamento, enquanto a indústria farmacêutica aceita receber pelo produto conforme o desempenho do medicamento em reais condições de uso. A partilha de risco depende, necessariamente, da coleta de evidências adicionais, que podem se referir aos benefícios terapêuticos ou ao volume de pacientes, conforme avaliação de seu uso na prática. Os autores descreveram a experiência do projeto-piloto de Acordo de Compartilhamento de Risco no Sistema Único de Saúde.

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Introduction

Law No. 8,080/1990, which established the Brazilian Unified Health System (SUS, in Portuguese), completed 30 years on September 19, 2020.

The advances were significant in expanding the coverage of primary care, the Brazilian National Immunization Program (PNI, in Portuguese), treatment of patients with HIV/AIDS/viral hepatitis, access to high-cost drugs, and overly complex procedures, with relevant impacts on outcome indicators in health. However, the Brazilian Unified Health System (SUS, in Portuguese) was conceived in the 1980s in a scenario of health care costs different from the current moment that diagnostic and therapeutic technologies took over a significant portion of the total health budget.

The uncritical incorporation of new health technologies, associated with the rise in the prevalence of non-communicable chronic diseases and population aging, is a determining factor in the increase in SUS costs. In this context, discussions regarding Health Technology Assessment (HTA) contribution to the formulation of health policies are increasingly relevant.

HTA aims to provide decision-makers with information about the possible impact and consequences of new technology on health or changes in established technology. It is responsible for assessing the direct and indirect effects, benefits and drawbacks, and mapping the steps involved in any technology transfer, both in the private and public sectors. The role of the HTA is to provide decision-makers with a hierarchical analysis of health policy options, with an understanding of the health, economic, environmental, social, political, and legal implications for society (Araújo *et al*., 2017).

In Brazil, the HTA process has been developed at an accelerated pace since 2004, when the Department of Science and Technology (DECIT, in Portuguese) was created, and the National Policy for Health Technology Management was approved. The Brazilian Network for Health Technology Assessment (REBRATS) was developed in 2007 to improve the government's regulatory capacity, define priority criteria, and disseminate the HTA study methodology. In 2011, Law No. 12,401, which amends Law No. 8,080, of 1990, regulated by Decree No. 7,646, of December 21, 2011, established the National Commission for Technology Incorporation (CONITEC) at SUS. Since then, HTA started to be used to support decision-making at SUS, supported by the legislation. Despite advances in HTA processes, there is a need to adopt new models for incorporating technologies, given the increased uncertainty about the benefits of new technologies and seeking greater budget predictability in the medium and long term.

Government's role in the acquisition of health technologies

The Brazilian Federal government plays several roles in the health area. The processes inherent to governmental activity have several components. One of the most important is public procurement management, including how the input acquisitions comply with the criteria of transparency, agility, and economy, subject to the highest possible competition (Giambiagi *et al*., 2020).

The Brazilian Federal government's purchase of general goods and services represents a considerable portion of the Gross Domestic Product (GDP). In the Organization for Economic Cooperation and Development (OECD) countries, this percentage was, on average, 12% in 2016. In the same period, Brazil represented 12.5% of GDP, 7.1% of which from the Federal Government (including state-owned enterprises and direct administration), 2.2% of states, and 3.2% of municipalities (Ribeiro *et al*., 2018).

Innovation in management to improve efficiency

A relevant issue concerns the process of innovation within governmental sectors, e.g., innovations in management processes (in the search for higher speed in serving the citizen and/or reduction of operational costs and risks), which is crucial for the provision of standardized services and on a large scale, such as health.

Social impact contracts – an instrument that transfers the risk of failure of pilot projects from governmental sectors to investors – are still hampered by Brazilian legislation.

Over the past decade, drug spending has increased rapidly and burdens more than other components of health care costs in many European countries and the United States (Adamski *et al*., 2010). One path taken in countries with universal access to health care systems was introducing new financing and payment modalities for innovative therapies.

One of the new modalities is the Risk-Sharing Agreement (RSA), defined as an agreement in which the Government agrees to offer access to a new therapy. At the same time, the pharmaceutical industry accepts to be paid for the product according to the drug's performance in its current conditions of use. Risk-sharing depends on collecting additional evidence, which may refer to the therapeutic benefits or the volume of patients, according to the evaluation of its use in practice.

Typically, some requirements are needed before these new types of agreements can become a realistic option in middle-income countries like Brazil. These requirements include: (i) a flexible legal framework, (ii) an adequate infrastructure for data collection within the country, for better assessment of all agreement points, (iii) potential for integration

between different databases for analysis of results, (iv) good alignment of objectives among health authorities, physicians and pharmaceutical industries, including appropriate incentives for all major stakeholder groups (Zampirolli *et al.*, 2020).

SUS's Experience with RSA

Given the severity of a rare disease called spinal muscular atrophy (5q SMA) and, consequently, the clinical and social relevance of ensuring access to the only medication approved in Brazil at that time, which altered the natural course of the disease, the Ministry of Health considered it positive and enriching to have a more in-depth discussion on the use of the RSA.

The use of RSAs to incorporate new technologies into health systems has become more common as governments seek alternatives to traditional forms of incorporation. This movement aims to ensure quick access to treatment for patients while reducing the government's risks for governments in offering relatively new high-cost technologies.

There are two options to use RSAs (Hauegen, 2014). They are divided according to the type of uncertainty they aim to face: the volume and budgetary impact or the product's clinical performance.

Volume-based risk-sharing agreement

Volume-based RSAs have been used longer and by more countries than clinical outcome-based agreements because they are more easily operationalized and focus primarily on the financial impacts of the therapy.

The decision to incorporate a drug is made based on an estimate of demand – based on the prevalence and incidence of the disease in the country –, which, in turn, makes it possible to calculate the budgetary impact of the technology. However, once used in the system, it is not uncommon for the effective demand for the drug to increase, mainly due to the lack of national data on the referred disease or the encouragement of diagnosis, since there is a new treatment option available.

In general, these are the cases where volume-based risk-sharing arrangements are adopted. The Government and the provider agree on a limit on expenditure, doses, patients seen, or treatment time, depending on the case. On the part of the Government, there is more management over demand growth and, consequently, more budget predictability. On the part of the company, the remuneration for the drug is subject to the risk of having to see more patients than initially planned. In this situation, the company can offer a differentiated price to the Government for additional treatment or even provide it at no extra cost. In this context, the manufacturer bears the risk of a financial impact by the demand increase, an expense that the public entity would previously pay.

Clinical outcome-based risk-sharing agreement

Clinical outcome-based RSAs are essential for real-life data generation and, therefore, to better understand available therapies in the market.

However, its operationalization is complex and costly. It requires the structuring or preparation of a network for performance assessment, clinical data management, and the involvement of patients, professionals, and health facilities during data collection. This model, particularly, requires a longer maturation time for its implementation.

The HTA process involves analyzing clinical evidence of the drug's safety, efficacy, and effectiveness. Such evidence, however, becomes more evident as its use is expanded beyond controlled trials in clinical research. Analyzes aiming to assess the product's cost-effectiveness and therapeutic value also tend to be strengthened once the technology starts to be used in the system.

In these cases, the technology's performance-based RSAs allow it to be offered to patients while making real-life evidence more robust. The agreement provides that the parties define what clinical uncertainty they want to resolve, such as target population, clinical performance, adverse effects, among others.

RSA pilot project at the Ministry of Health of Brazil in 2019-2020

Phase 1 – Mitigation of financial risks and access to Spinraza® (Nusinersen)

Objective

Ensure timely access to patients with 5q SMA, including those not included in the SCTIE Ordinance No. 24/2019, and at the same time mitigate the financial risk for the Ministry of Health arising from uncertainties about the epidemiology of the disease during the period of structuring the RSA model.

Activity proposal

- Incorporation of Spinraza® (Nusinersen) for type 1 SMA following the traditional patterns of incorporation and acquisition of health technologies at SUS.
- Incorporation of Spinraza® (Nusinersen) for late-start 5q SMA subject to the RSA and with a financial risk mitigation model in the first year of incorporation, during the structuring of the RSA model, valid as from the second year of incorporation.

At this phase, a limit of patients and/or bottles to be purchased by the Ministry of Health was established. The other bottles would be provided free of charge by the pharmaceutical industry that produces Spinraza® (Nusinersen). A second limit can be negotiated, at which cost-free bottles will no longer be supplied, and supply conditions will be renegotiated.

Phase 2 – Structuring the RSA by the outcome

Objective

Structure the RSA model by the outcome and ensure the existence and implementation of all the required structures to execute the agreement.

Description

In parallel with establishing the budget limit model and 5q SMA patients' access, it is proposed to define all principles and criteria for structuring the agreement by the outcome and preparing reference centers responsible for collecting the results to be analyzed.

Activity proposal

1. Definition of RSA's outcomes and conditions

A discussion group was organized with specialist physicians, a multidisciplinary team, and representatives of the patient community to generate a broad and integrated understanding of the disease and to collect information about the relevance of different clinical outcomes that support the definition of outcomes to be adopted in the RSA by the outcome.

Still, after defining the outcomes, the agreement conditions to be signed have also been discussed. They were as follows: expected clinical results for the selected outcomes, value, and reimbursement terms to be granted in case of failure to achieve the result defined as the objective [as free bottles, or another model to be decided along with the Ministry of Health and the pharmaceutical industry that produces Spinraza® (Nusinersen)], minimum follow-up time per patient to analyze the achievement of expected outcomes and dates for their evaluation. For the follow-up and assessment of patients with 5q SMA, the model suggested for structuring the RSA is that of a patient record capable of receiving information about the characteristics of patients with the disease and measuring the previously defined outcomes.

2. Assessment of patient care reference centers

This phase included assessing the main 5q SMA care centers in Brazil, their geographic distribution, and the conditions for diagnosing, treating, and providing multidisciplinary support to patients.

A survey carried out at the end of 2018 identified 59 institutions across the country that monitor patients with 5q SMA, with the highest concentration in the Southeast and South regions (69%), but with locations also in the Central-West and Northeast regions. Among them, 71% are public institutions, 21% are public and private, and 8% are private institutions. Currently, 32% already administer the drug regularly. Another 34 institutions do not monitor the patient but are able to carry out the drug administration or multidisciplinary procedures (e.g., physiotherapy, rehabilitation, etc.). Currently, in Brazil, the scope of this global care varies from place to place and from region to region.

Considering Brazil's continental dimension and aiming to ensure a quick and viable implementation of the RSA project for Spinraza® (Nusinersen), it is proposed to develop a pilot analysis. It will involve the main reference centers in the country with a physical structure, information technology infrastructure, multidisciplinary professionals trained at the end of the first year of the project, and whose results are extrapolated to the population undergoing treatment with Spinraza® (Nusinersen). This analysis in the main centers would not prevent the construction of the patient record at the federal level. Still, it would facilitate the audit and guarantee the adequate training of professionals responsible for capturing and inserting information to evaluate the outcomes obtained about the expected results for the treatment.

3. Operationalization

Genetic test

The diagnosis of 5q SMA is genetically defined through the MLPA test (multiplex ligation-dependent probe amplification) or qPCR (quantitative polymerase chain reaction) and sequencing to the detection of compound heterozygotes (Mercuri *et al.*, 2018). Since 2018, the pharmaceutical industry that produces Spinraza® (Nusinersen) has offered MLPA testing to medical professionals through its patient support program.

Multidisciplinary team education

The care of 5q SMA patients should ideally include professionals from different areas working in an integrated manner (pediatric, neurology, neuropediatric, intensive care, pulmonology, anesthesiology, orthopedic, clinical nutrition, nutrition, motor and respiratory physiotherapy, psychology, occupational therapy, speech therapy, genetics, nursing, among others).

Continuing education topics: 5q SMA (clinical, epidemiology), diagnosis of 5q SMA and family genetic counseling, the guidance of caregivers, monitoring of motor and respiratory functions by qualitative clinical assessments and validated scales, respiratory and motor care in a proactive and reactive context, intensive care in urgencies and emergencies, care in the administration of Spinraza® (Nusinersen), insertion of the person with 5q AME in the society, nutritional care, among others. Among these topics, essential outcomes, and evaluations for assessing disease progression and response to the treatment were discussed in the context of the natural history of 5q SMA.

The proposed format was based on online platforms available on the internet, with classes filmed and edited in advance and made available as webinars. The classes would be prepared by specialists from different areas with vast experience in neuromuscular diseases and in 5q SMA, specifically.

Except for the one on pharmacological treatment, the themes would be made available to all professionals involved

in caring for people with 5q SMA. Regarding the pharmacological treatment topic, it would be available to professionals qualified to prescribe and dispense medication.

Phase 3 – Elaboration of the RSA contract

Objective

The drafting of a new contract, specific to the RSA model, is based on the previous phase's outcomes. It is important to note that the Ministry of Health and the pharmaceutical industry that produces Spinraza® (Nusinersen) understand that risk-sharing is exclusively an agreement between the manufacturer and the paying source and should not fall, in any way, on the patient community.

Description

To ensure transparency and reliability and provide legal certainty for both parties, a robust contract would be built with which everyone is comfortable and clear. This contract should contain clauses referring to the defined outcomes for the assessment, duration of the RSA, closing criteria, transparency, and data protection, among others until all relevant points had been exhaustively discussed.

Activity proposal

The contract drafting should be carried out by the legal entity of each of the parties, with the assistance of medical and multidisciplinary specialists.

Those responsible for measuring the outcomes agreed between both parties must be defined in a contract. How such results will be collected must be described in detail, and clauses relating to monitoring the progress of the project and those responsible and how the data collected will be audited.

It is essential that the RSA drafting define the deadlines for each phase to be completed, for the outcome assessments to be collected, and for the outcome assessment to be carried out. The deadline for completing the contract and price review, suggested here after two years after the start of the RSA by the outcome, must also be established in the contract.

Criteria for the contract termination by both parties will also need to be defined and established in the contract.

The start of the RSA contract should be related to the end of the volume pricing procurement model. It will only be implemented in the first year of the project.

A working group (and those responsible for each party) was also determined to carry out periodic monitoring of the project's progress and define the responsibilities of each member of the group in ensuring compliance with each process and the quality of the project.

Considering the data to be evaluated, it was also suggested such data be anonymized and made public to ensure the transparency of the process and the safety for analyzing the outcomes obtained concerning the expected results. It was also recommended that there be an independent entity responsible for auditing and evaluating the data collected.

Phase 4 – Information Collection

Objective

Start recording the outcomes and information to be evaluated in the RSA at the defined reference centers.

Description

The collection of information should start within one year at the latest after incorporating the drug to guarantee an appropriate follow-up time for analyzing defined outcomes.

Activity proposal

All centers designated for the collection of outcomes will start recording data as soon as they are fully trained for this activity. All centers chosen for the pilot analysis must be prepared at the beginning of the first year of the RSA's validity, and all other centers must be able to start collecting on the first day of the third year of the project (second of the RSA).

Information recording must be kept confidential until the first reading, at the end of the first year of the RSA by the outcome, to ensure the impartiality of the analysis of the collected results. The periodic evaluation of the working group responsible for monitoring the project's execution and progress will also be of great importance to identify possible failures, lack of technical training, or practices that could generate biases or impair the analysis of previously defined outcomes.

The last collection to be used for the final analysis of outcomes and for defining the responsibilities of each party involved in the RSA should take place on the last day of the second year of the RSA.

Phase 5 – Analysis of outcomes

Objective

Evaluate the performance of Spinraza® (Nusinersen) in patients with later types of disease concerning the expected results for the product and define the responsibilities of the parties involved in the contract.

Description

At the end of the first year of RSA, an interim analysis will be carried out to identify the performance of Spinraza® (Nusinersen) and possible price renegotiation. At the end of the second year of RSA and consequent contract termination, the parties involved must define whether the expected outcomes have been achieved, in what proportion, and whether there will be a need for a retroactive discount. At this phase, the purchase price can be discussed again.

Proposed activities

Although patient assessment and data collection are carried out individually, patient by patient, it is suggested that the analysis of outcomes be carried out at the population level. The rationale is to establish the number of patients who should respond to treatment (according to predefined outcomes). In the end, the result is compared to the percentage of those patients who responded.

It is worth emphasizing that the definition of the criteria considered as a response to the treatment must have the function of determining the financial reimbursement (or not) based on the expected outcomes. An independent entity must analyze results to develop the statistical evaluation of the outcomes (Clinical Research Organization or CRO, for example), both at the end of the first year and the end of the second year of the RSA.

After each analysis, the risk-sharing criteria previously defined in the contract must be met. If the outcomes evaluated are below expectation for the product, a retroactive discount must be provided, granted through the purchase of bottles at no cost.

Phase 6 – Review of the Clinical Protocol and Therapeutic Guidelines (PCDT, in Portuguese)

Objective

Identify, from the assessed outcomes, whether it is required to update the PCDTs, restrict access to the drug to any subpopulation based on its performance concerning what was expected, or expand access to a more significant portion of patients without the need for the RSA maintenance.

Description

At the end of the evaluation of outcomes and if compensation to the government for performance below the established level is required, it is suggested assessing, more depth, which subpopulations may have presented an inadequate response to the drug and which, therefore, justified the review of the federal protocol initially established.

Proposed activities

Qualitative, quantitative, and statistical analyses of subgroups of patients with similar profiles should be performed based on variables that a group of specialist physicians may suggest defining possible criteria for excluding patient profiles from the protocol.

Legal evaluation for the RSA at SUS

One of the most critical phases in drafting the RSA pilot project was the appreciation of the Legal Advisory of the Ministry of Health (CONJUR-MS, in Portuguese) on the topic. CONJUR-MS recognized that uncertainty regarding treatment performance under actual conditions of use is considered one of the most significant challenges for public health. However, the greatest challenge faced by the Ministry of Health was the absence of a normative forecast that anticipated and prepared the system for the RSA.

In the initial phase of the pilot project, CONJUR-MS assessed that concerning the "Risk-Sharing Agreement - RSA" compatibility with the legal-normative framework that governs the SUS, there was no legal obstacle to its implementation and use for the incorporation of health technologies.

Regarding the institution of a "Pilot Project" for the RSA, it was understood as a prudent measure since it is an unprecedented situation. Caution and exceptionality in its use are recommended.

Therefore, about the constitutionality and legality of the ordinance draft under analysis, the Legal Counsel understood that there are no legal obstacles to the continuity of the process and its edition, considering the technical inputs contained in the records.

However, CONJUR-MS recommended that the execution of the pilot project should necessarily be preceded by the incorporation of the drug Spinraza® (Nusinersen) for the treatment of types II and III SMA, in compliance with the rules introduced by Chapter VIII of Law No. 8,080/1990.

Given this recommendation by CONJUR-MS, the Ministry of Health's Department of Science, Technology, Innovation and Strategic Inputs (SCTIE-MS) conducted the pilot project. It was characterized as a research project, with submission to the research ethics committees of the health centers reference, to the end of the proposed period, with the evidence analyzed, submit to CONITEC's evaluation for its incorporation or not.

Conclusion

The experience with RSA at the Ministry of Health indicated strengths and bottlenecks for implementing this model at SUS. As for strengths, we can list the existence of infrastructure and specialized human capital for assistance and research in reference centers in Brazil; the managerial capacity of SCTIE/MS technicians to plan and monitor the execution of the RSA; the receptiveness of the pharmaceutical industry to carry out this type of agreement. The biggest bottleneck for implementation is the current legal framework, which prevents SUS from acquiring technologies.

The debate on the RSA pilot project at the Ministry of Health involved academics, managers, public policy makers, parliamentarians, regulators, oversight bodies, and civil society.

Below is the conclusion of the master's thesis "Risk-sharing agreements for the acquisition of drugs by the government to supply the SUS: legal analysis in the light of the case of the nusinersen product", carried out at the São Paulo Law School of Fundação Getúlio Vargas (Ueno, 2020):

- "The future general standard will regulate risk-sharing agreements for incorporating health technologies at SUS, based on the nusinersen pilot project, should establish detailed governance rules and management procedures to prevent conflicts of interest, and a clear delimitation of the extent for using risk-sharing agreements, restricting it to situations involving innovative drugs with the high cost and technological content. It is a topic that generates large financial liabilities to the Government, i.e., it should be applied as a special regime for specific purposes".
- "To ensure good faith, transparency, and legal certainty for the parties, the instrument formalizing the clinical outcomes defined for the assessment, duration of the agreement, closing criteria, transparency and data protection, and all other issues relating to risk-sharing."
- "A formal governance structure is essential to ensure the transparency of the risk-sharing nature and objectives, accountability rules, and means to mitigate possible conflicts. since, as explained, there will be the involvement of different parties motivated by different interests and need to measure highly complex results."
- "It is important to emphasize that the issue of data collection is fundamental and should be thought through with caution, as sensitive and confidential data (both from the industry regarding the intellectual property of the technology and from patients regarding their health status) will be collected and treated. The conditions and terms for data collection and processing must be specified (who will hold them, who could publish them, how the results will be treated and processed, etc.)".
- "Certainly, the adoption of innovative and complex models, such as the risk-sharing agreement in the health field, will be simpler and safer when the specific legislation that protects it is enacted."

There is a need to reform the Brazilian Federal Government to improve public management efficiency and maximize the use of resources under conditions of uncertainty, such as, e.g., the public health scenario. As the Nobel Memorial Prize in Economic Sciences, Jean Tirole states, "reforming the Government means transforming it into an instrument that will put the economy to work for the common good" (Tirole, 2020).

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